Dr. William S. Stokes
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October 19, 2004

Re: Meeting of the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) on October 20, 2004
The Importance of Method Validation within NTP's Roadmap/Vision for the 21st Century

Dear Dr. Stokes,

The American Chemistry Council strongly supports the mission of the Interagency Coordinating Committee for Validation of Alternative Methods (ICCVAM). For over three decades the American Chemistry Council (ACC or the "Council") and its member companies have played an active role in both screening and testing chemical substances and in the development of alternative toxicity test methods.[1]

For close to a year now, the National Toxicology Program (NTP) has been engaged in stakeholder dialogues focused on obtaining feedback on NTP's Vision for the 21st Century. We support the efforts by NTP to involve stakeholders in this important process in considering how to address the challenges faced in expanding, and perhaps refocusing, NTP's toxicological testing and research efforts to make more use of mechanism-based biological tools.
While early drafts of NTP's Roadmap and Vision documents did not include much detail or focus on the importance of method validation, the more recent reviews/reports by the NTP Participating Agencies and the NTP's Board of Scientific Counselors Subcommittee and the

[1] The American Chemistry Council represents the leading companies engaged in the business of chemistry. ACC members apply the science of chemistry to make innovative products and services that make people's lives better, healthier and safer. ACC is committed to improved environmental, health and safety performance through health and environmental research and product testing, Responsible Care®, and common sense advocacy designed to address major public policy issues. The business of chemistry is a $460 billion enterprise and a key element of the nation's economy. It is the nation's largest exporter, accounting for ten cents out of every dollar in U.S. exports. Chemistry companies invest more in research and development than any other business sector. Safety and security have always been primary concerns of ACC members, and they have intensified their efforts, working closely with government agencies to improve security and to defend against any threat to the nation's critical infrastructure.

NIEHS Committee for Development of the NTP Vision point out the need for NTP to integrate method validation into its programs.

The Council has repeatedly urged NTP and the National Institute of Environmental Health Sciences (NIEHS) to make better use of ICCVAM to review and evaluate alternative methods. The ICCVAM Authorization Act of 2000 (42 U.S.C. 2851) operates to ensure that any new or revised acute or chronic toxicity test method, including animal test methods and alternatives, is determined to be valid for proposed use prior to an Agency requiring, recommending, or encouraging the application of such test method. In moving forward with development and standardization of new, revised and alternative methods, NTP and NIEHS have an obligation to fully integrate method validation work into their program efforts.

In developing new, revised and alternative methods, including those focused on mode or mechanism of action, NTP and NIEHS should fully embrace validation studies, because these investigations provide the critical scientific data and information needed to understand the relevance, reliability, and appropriate use of such methods. Since the use of new, revised or alternative methods developed or applied by NTP/NIEHS is likely to have widespread impact across various health and environmental programs in a multitude of Federal agencies, we believe that in the spirit of the ICCVAM statute, NTP should sponsor and support appropriate method validation studies. Omission of such would be inconsistent with the ICCVAM Authorization Act of 2000.

NTP is well positioned both to validate new, revised and alternative methods and to catalyze scientific investigations, dialogue and consensus to better understand the relationship between mechanistic biological observations and adverse health effects. To move in this direction, NTP will need to develop a framework for relating mechanism-based data to the more traditional in vivo studies in order to demonstrate the appropriate use of mechanistic data in extrapolation and quantification of risk to humans. In this regard, NTP will need to build the frameworks to enable predictive methods or batteries to be interpreted in light of the nature, relevance and reliability of the assay/battery. Because toxicity can only be appropriately understood within the context of dose, NTP should prioritize efforts that facilitate extrapolation from model systems to humans, in a manner that recognizes and accounts for dose-dependency and species similarities/differences.

In moving forward with the NTP Vision and Roadmap, the Council believes it is necessary for NTP to focus on its unique role and capabilities among federal agencies' and laboratories. NTP/NIEHS is well situated to address some of the areas pertaining to advancing the use of mechanistic data/information in risk assessment, but not all. It remains unclear how and to what extent the Vision would change the role of NTP in risk assessments, and whether this would be duplicative or encroach upon other agencies missions. The Council agrees that as NTP moves forward and its goals and objectives become more crystallized, the NTP/NIEHS must articulate these goals, develop a draft strategy to achieve the goals, and have these drafts reviewed and discussed in scientific and stakeholder forums prior to initiating the efforts.

We believe it is important for the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) to continue to support and strengthen ICCVAM as the focal point within NIEHS and the Federal government to coordinate cross-agency issues relating to development, validation, acceptance, and national/international harmonization of new, revised and alternative toxicological test methods. As NTP and NIEHS move forward, the SACATM has an important role to play in recommending how method validation should be integrated within NTP's programs and coordinated across agencies. We look forward to continued progress within NTP/NIEHS and other Federal Agencies on the development, standardization and validation of alternative toxicity test methods. Please don't hesitate to contact me by e-mail (Rick_Becker@americanchemistry.com) or by phone (703-741-5210) should you wish to discuss any of these matters in greater detail.

Sincerely,

Original Signed By

Richard A. Becker, Ph.D., DABT
Public Health Team

cc Dr. Kristina Thayer, NTP Liaison and Scientific Review Office, National Institute of Environmental Health Sciences, P.O. Box 12233, Research Triangle Park, NC 27709